Abstract

A prokaryotic recombinant host cell comprising a heterologous replication initiation protein that activates a conditional origin of replication and an extrachromosomal DNA molecule comprising a heterologous therapeutic gene and a conditional origin of replication whose functionality in the prokaryotic recombinant host cell requires a replication initiating protein which is foreign to the host cell is described. The host cell may comprise a *pir* gene having at least one mutation, which may occur in the *pir* gene copy number control region, the *pir* gene leucine zipper-like motif, or the *pir* gene DNA binding region.